FDA Anthrax Preparedness

Improving a Path Forward: New Steps in Anthrax Planning

Public Health Preparedness Summit

Anaheim, CA

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CAPT Carmen Maher, BSN, MA, RN, RAC
Deputy Director (Acting)
Office of Counterterrorism and Emerging Threats
Office of the Commissioner
U.S. Food and Drug Administration

Overview

- FDA Anthrax Preparedness
  - Overarching Functions
  - Development, Approval, and Use of medical countermeasures (MCMs)
  - Regulatory Mechanisms for development and use of MCMs
  - Public Health Emergencies vs. Product Development and Clinical Research
- FDA Response Planning and Execution
  - EUAs for Anthrax Preparedness and Response
  - FDA Response Structure
  - Linkage and communication with HHS, CDC, and other stakeholders

Overview of MCM Functions

- Overarching functions
  - Review and approval
  - Enforcement
  - Communication
- Centers (CDER, CBER, CDRH)
  - Product-specific scientific and technical expertise
  - Objective regulatory review
  - Early engagement with product developers
- Office of Counterterrorism and Emerging Threats (OCET)

Office of Counterterrorism and Emerging Threats (OCET)

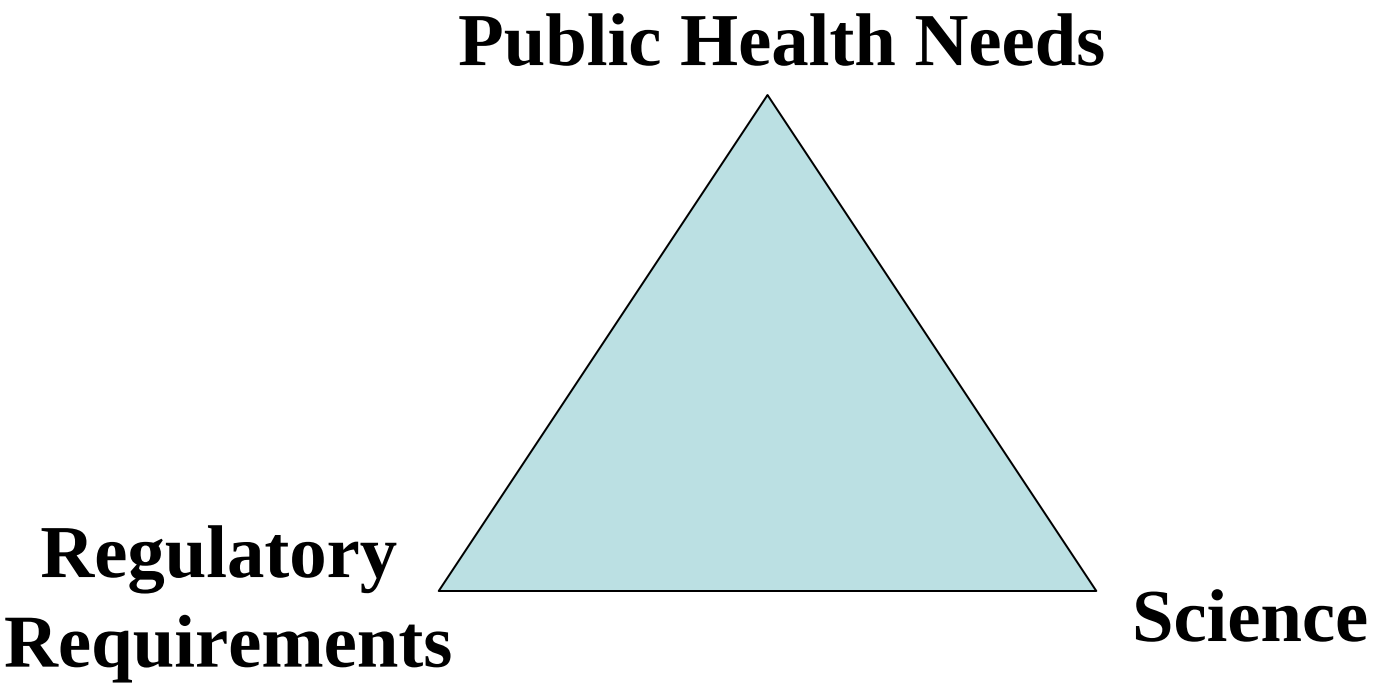
Facilitates development and availability of safe and effective public health emergency MCMs

- Identifies and resolves complex scientific and regulatory challenges facing MCM development, approval, availability, and security
- Leads Emergency Use Authorization (EUA) activities
- Coordinates the Medical Countermeasures Initiative (MCMi)
- Collaborates with Centers and Offices, and external partners, to develop and coordinate implementation of preparedness plans and programs to counter emerging threats

Regulatory Mechanisms for Development and Emergency Use of MCMs:

Investigational New Drug (IND) Application
or
Investigational Device Exemption (IDE)
and
Emergency Use Authorization (EUA)

FDA's MCM Balance



PHE vs. R&D

Public Health Emergency	Research & Development
•Intent – respond and mitigate	•Intent - Generalizable Knowledge
•Unplanned/Unexpected	•Planned/Deliberate
•Chaos or controlled chaos	•Well controlled clinical trials
•Large numbers of individuals	•Smaller numbers of individuals
–Simultaneous administration	–Stepwise progression
•Rapid decision making/response	•Careful decision making/time
•Limited information dissemination	•Informed Consent/Process
•Little or no tracking/monitoring	•IRB review and approval
	•Strict oversight/monitoring

Anthrax incident MCM response will blur these lines

INDs and IDEs

- To be used in human testing in the U.S., in most cases:
  - A drug, including a biologic drug, must be covered by an IND (FD&C Act § 505(i), 21 CFR §312.20)
  - A device must be covered by an IDE (FD&C Act §520(g), 21 CFR §812.20)
- INDs and IDEs are reviewed by FDA, which has the authority to halt investigations proposed to be carried on under these applications
- IND and IDE regulations require patient safeguards, including in most cases Institutional Review Board (IRB) supervision of investigations, informed consent by subjects, and reporting to FDA

INDs: Emergency Use of Investigational Products

- In some circumstances, an IND (or IDE) may be the most appropriate mechanism for use of an unapproved product during an emergency
- For example, FDA regulations permit the use of investigational drugs for serious or life-threatening diseases or conditions in certain circumstances:
  - Emergency use IND for individual patients (21 CFR §312.20)
  - Expanded access trial under an IND (for intermediate-sized patient populations) (21 CFR §312.315)
  - Treatment IND or treatment protocol under an IND (21 CFR §312.320)

EUAs

- Section 564 of the Federal Food, Drug, & Cosmetic Act, as amended by the Project BioShield Act (2004)
- In an emergency, the risk-benefit analysis may change
- If FDA grants a request for an EUA, it is finding that, in a particular type of emergency, if the conditions set out in the EUA are observed:
  - An approved product may be used in a way inconsistent with the limitations of the approval, or
  - A product that has not yet been approved may be permitted to be used (despite lacking the quantum of data that would be necessary for a full approval)

When an EUA?

- Novel/investigational products may be the best available to meet emergency needs
- Requirements for clinical investigations or expanded access would be difficult to meet in emergency mass dispensing scenario AND data supports use under EUA
- Changes from approved labeling, expiration dating, dosing schedule, and prescribing requirements would render the product misbranded or unapproved
- Potential gap for PREP Act liability coverage exists
  - PREP Act declarations can cover MCMs for which EUAs have been issued during an emergency

Criteria for Issuing an EUA

- Serious or life-threatening illness or condition caused by CBRN agent
- Reasonable belief product may be effective
- Known/potential benefits outweigh known/potential risks
- No adequate, approved, available alternative to product
- Other factors FDA considers:
  - Public health need
  - Circumstances of the emergency
  - Product's regulatory status
  - Safety and efficacy data
  - Product quality, shelf life, storage
  - Operational issues

EUA Conditions of Authorization

- Address elements of the Authorization, such as:
  - Emergency use information (e.g., fact sheets, modified dosing)
  - Dispensing/screening procedures
  - Record keeping and monitoring of adverse events
  - Waiver of cGMP requirements
- Clarify roles
  - e.g.) for CDC, state and local public health departments, private sector stockpilers, etc.
- Because use of a product under an EUA is not investigational, IRB approval and informed consent are not required; also, alternative dispensing mechanisms can be authorized

Anthrax Vaccine

- Anthrax Vaccine Adsorbed (AVA)
  - Vaccine licensed by FDA for adults (18 – 65 yrs) and limited to for those at high risk for exposure to anthrax; not for PEP
  - No safety or efficacy data for pediatric populations (<18 years of age) or pregnant women
- Response Considerations
  - Proposed 3-dose regimen, plus 60 days of approved antibiotics
  - *Adult populations*: Use under an EUA
  - *Pediatric populations*: Use under an Investigational New Drug (IND) application
    - Informed consent requirements because of lack of clinical data in pediatric populations (so cannot determine whether the "*known and potential benefits outweigh the known and potential risks*")

EUA Activities

- DoD (anthrax vaccine) (2005) (*expired*)
- H1N1 Influenza Pandemic (2009) (*expired*)
  - Drugs (antivirals) (multiple EUAs)
  - Devices (IVDs) (multiple EUAs)
  - PPE
- Mass Dispensing (doxycycline) (2011) (*current*)
- National Postal Model (doxycycline kits) (2011) (*current*)
- Pre-EUA activities (*ongoing*)

FDA Response Planning and Execution

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LCDR Anthony (Tony) Garza, MS
Senior Program Manager
Office of Counterterrorism and Emerging Threats
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FDA's Anthrax Preparedness and Response

- Doxycycline Mass Dispensing EUA
- National Postal Model (NPM) EUA
- FDA's role as a response Agency

Doxycycline Mass Dispensing EUA

- 2011: CDC submitted an EUA request to FDA for oral formulations of doxycycline products for inhalational anthrax to facilitate stakeholders' preparedness and response activities
- This EUA was possible because of:
  - DHS Secretary's determination of significant potential for a domestic emergency involving *B. anthracis* (2008)
  - HHS Secretary's declaration of emergency justifying the authorization of emergency use of doxycycline hyclate tablets for post-exposure prophylaxis (PEP) (2008, 2009, 2010)
  - HHS Secretary's renewal and amendment of the above HHS declaration to apply to all oral formulations of doxycycline (July 20, 2011)

Doxycycline Mass Dispensing EUA

- Issued July 21, 2011
  - Covers oral formulations of doxycycline (capsule, tablet, and liquid formulations), including partial supplies (e.g., 10-day supply), for PEP of inhalational anthrax
  - Facilitates preparedness and response activities, which may otherwise violate provisions of the FD&C Act. For example:
    - Authorizes dispensing without a prescription and accompanied by authorized emergency use information
    - Sets forth “minimum elements” to provide flexibilities in developing informational materials (e.g., fact sheets) for health care professionals and for recipients
- For additional information, refer to Letter of Authorization: http://www.fda.gov/downloads/EmergencyPreparedness/Counterterrorism/UCM264104.pdf

National Postal Model (NPM) EUA

- 2008: FDA issued the 1st EUA for doxycycline hyclate tablets (for inhalational anthrax) contained in individual workplace and household emergency antibiotic kits (HAKs) for eligible USPS employee volunteers in the CRI/Postal Model and their household members
  - EUA amended and reissued in 2009 and 2010
- 2011: ASPR/BARDA submitted a request to FDA to amend the existing Postal Model EUA to reflect programmatic and operational changes, such as:
  - Updating information and screening materials
  - Removing references to PPE
  - Changing references to program name from “CRI” to “NPM”

National Postal Model (NPM) EUA

- The 2011 EUA was possible because of:
  - DHS Secretary's determination of significant potential for a domestic emergency involving *B. anthracis* (2008)
  - HHS Secretary's renewal and amendment of HHS declaration of emergency justifying the authorization of emergency use of doxycycline hyclate tablets for PEP (2008, 2009, 2010) to apply to all oral formulations of doxycycline (July 20, 2011)
- Issued October 14, 2011
  - Covers doxycycline hyclate tablet emergency kits ("HAKs") for PEP of inhalational anthrax
  - Limited to HAKs for eligible USPS employee volunteers in the NPM and their household members, based on the request

National Postal Model (NPM) EUA

- Facilitates NPM preparedness and response activities, which may otherwise violate provisions of the FD&C Act. For example, authorizes:
  - Distribution and use of emergency use information sheets (e.g., fact sheets for recipients)
  - Dispensing without all required prescription label information
  - Dispensing of partial supply of full 60-day dosage regimen
  - Pre-event storage or distribution
- For additional information, refer to Letter of Authorization:
  - http://www.fda.gov/downloads/EmergencyPreparedness/Counterterrorism/UCM277222.pdf

FDA Office of Crisis Management

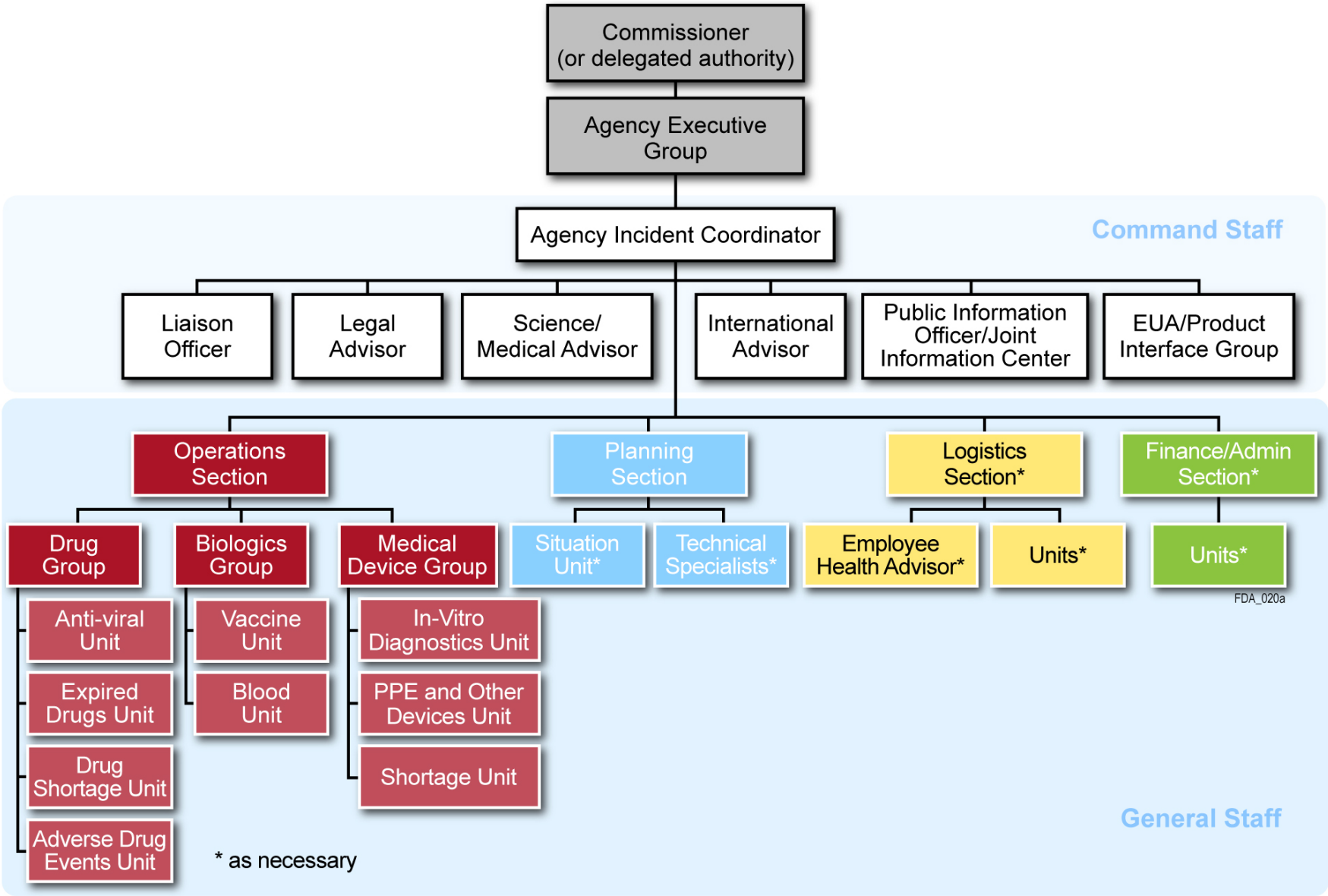
- Agency focal point for coordinating responses to crises/emergencies
- Crisis/emergency management policies and programs
- Agency liaison to HHS Secretary's Operations Center and other Emergency Operations Centers
- Agency representative for International Health Regulations Workgroup, DHS Interagency Operations Centers Workgroup, G8 Exercise Planning Group, U.S./Canada/Mexico Trilateral Cooperation Emergency Preparedness and Response Workgroup and other national/international groups
- Internal/external security and other related activities

Office of Crisis Management
Office of Emergency Operations

- FDA's Emergency Operations Center (EOC) – 24/7 emergency response system
- Internal and external CT/emergency exercises
- FDA Emergency Response Plans – BSE, Chem-Bio, Radiological, Pandemic Influenza
- Coordinate emergency/ICS training for agency staff
- Emergency Operations Network Information Management System (EON IMS)
- National Consumer Complaint System
- FDA 24 Hour Number (Emergency) **1-866-300-4374**

www.fda.gov/EmergencyPreparedness

FDA CBRN Response Structure


Commissioner (or delegated authority)
Agency Executive Group
Agency Incident Coordinator
Command Staff
Liaison Officer
Legal Advisor
Science/ Medical Advisor
International Advisor
Public Information Officer/Joint Information Center
EUA/Product Interface Group
Operations Section
Planning Section
Logistics Section*
Finance/Admin Section*
Drug Group
Biologics Group
Medical Device Group
Situation Unit*
Technical Specialists*
Employee Health Advisor*
Units*
Units*
Anti-viral Unit
Expired Drugs Unit
Drug Shortage Unit
Adverse Drug Events Unit
Vaccine Unit
Blood Unit
In-Vitro Diagnostics Unit
PPE and Other Devices Unit
Shortage Unit
FDA_020a
General Staff
* as necessary

FDA Resources

- State & Local Stakeholder Site
  - http://www.fda.gov/EmergencyPreparedness/Counterterrorism/ucm234336.htm
- EUA Questions & Answers
  - http://www.fda.gov/NewsEvents/PublicHealthFocus/ucm153297.htm
- EUA Guidance
  - http://www.fda.gov/RegulatoryInformation/Guidances/ucm125127.htm
- Current & Past EUAs
  - http://www.fda.gov/EmergencyPreparedness/Counterterrorism/ucm182568.htm
- Medical Countermeasures Initiative (MCMi)
  - www.fda.gov/medicalcountermeasures
- FDA Emergency Operations Plan (EOP)
  - http://www.fda.gov/EmergencyPreparedness/EmergencyPreparedness/default.htm

Additional Resources

- Institute of Medicine, *Medical Countermeasures Dispensing: Emergency Use Authorization and the Postal Model: Workshop Summary* (2010) (http://www.nap.edu/catalog/12952.html).

- Sherman S.E., Foster J., Vaid S., Emergency use authority and 2009 H1N1 influenza. *Biosecur Bioterror* 2009;7(3):245-250.

- Quinn S.C., et al., Public willingness to take a vaccine or drug under emergency use authorization during the 2009 H1N1 pandemic. *Biosecur Bioterror* 2009;7(3):275-290.

- Birnkrant D., Cox E., The emergency use authorization of peramivir for treatment of 2009 H1N1 influenza. *NEJM* 2009; 361(23):2204-2207.

Contact Information

CAPT Carmen Maher
Deputy Director (acting)
Office of Counterterrorism and Emerging Threats
Office of the Commissioner
Food and Drug Administration
301.796.8510
carmen.maher@fda.hhs.gov

LCDR Anthony Garza
Senior Program Manager
Office of Counterterrorism and Emerging Threats
Office of the Commissioner
Food and Drug Administration
301.796.8510
anthony.garza@fda.hhs.gov

MCMi Website: www.fda.gov/medicalcountermeasures

EUA.OCET@fda.hhs.gov

Thank you!